Complete Summary

GUIDELINE TITLE

2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology.

BIBLIOGRAPHIC SOURCE(S)

Bast RC, Ravdin P, Hayes DF, Bates S, Fritsche H, Jessup JM, Kemeny N, Locker GY, Mennel RG, Somerfield MR. 2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001 Mar 15;19(6):1865-78.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Breast cancer
- Colorectal cancer

GUIDELINE CATEGORY

Diagnosis
Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To update established practice guidelines for the use of tumor marker tests in the prevention, screening, treatment, and surveillance of breast and colorectal cancers

TARGET POPULATION

Patients with or suspected of having breast or colorectal cancer.

INTERVENTIONS AND PRACTICES CONSIDERED

All commonly used circulating and tissue-based markers in the care of breast and colorectal cancer patients were evaluated.

Colorectal Cancer Diagnostic Tests:

1. Serum carcinoembryonic antigen (CEA)
2. Serum lipid-associated sialic acid (LASA)
3. Serum cancer antigen (CA) 19-9
4. DNA flow cytometric ploidy (DNA index)
5. DNA flow cytometric proliferation index (% S phase)
6. p53 Tumor suppressor gene
7. ras oncogene

Breast Cancer Diagnostic Tests:

1. Serum CA 15-3 (also CA 27.29: Tru-Quant BR RIA test [Biomira Diagnostics, Toronto, Canada])
2. Serum CEA
3. Estrogen and progesterone receptors
4. DNA flow cytometric ploidy (DNA index)
5. DNA flow cytometric proliferation index (% S phase)
6. p-53 Tumor suppressor gene
7. c-erbB-2
8. Cathepsin-D

MAJOR OUTCOMES CONSIDERED

- Overall survival
- Disease-free survival
- Toxicity
- Quality of life
- Cost-effectiveness of care

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developers performed a computerized literature search using Medline (U.S. National Library of Medicine). Key words included the disease (colorectal or breast carcinoma) and the marker in question. In addition to reports collected by individual Panel members, all articles published in the English-speaking literature from January 1989 to April 1994 were collected for review and distributed to all members of the Panel.

1997 Update: The guideline developers conducted a computerized literature search from 1994 to July 1997.

2000 Update: The guideline developers conducted computerized literature searches of the Medline and CancerLit databases. The searches of the English-language literature from 1994 to 1999 combined each of the markers with the corresponding disease site.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

A modification of the scale developed by the Canadian Task Force on the Periodic Health Examination was used:

Level I: Evidence from meta-analysis or large, high-powered concurrently controlled studies in which the primary objective of the trial design was to test the utility of the marker.

Level II: Evidence was obtained from prospective clinical trials designed to test a therapeutic hypothesis in which tumor marker evaluation was a secondary, but prospectively described objective.

Level III: Studies were retrospective, but characterized by large size (greater than 200 patients per subgroup) and/or by inclusion of multivariate analysis.

Level IV: Evidence was considered less reliable than level III evidence, either because the study was smaller or a multivariate analysis was not provided.

Level V: Evidence was derived from studies that were small, retrospective, and not designed to correlate marker results with clinical outcome.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Values for use, utility, and levels of evidence were assigned by the expert reviewers and approved by the Panel. For each potential use, the Panel determined a utility score of the marker for one or more potential outcomes.

For the 2000 update, an update committee composed of members from the full panel was formed to review and to analyze data published since 1994. The update committee had a single face-to-face meeting to consider the evidence for each of the 1997 recommendations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Values for use, utility, and levels of evidence were assigned by the expert reviewers and approved by the Panel. For each potential use, the Panel determined a utility score of the marker for one or more potential outcomes. See also the "Type of Evidence Supporting the Recommendations" field.

The guideline was circulated in draft form to the update committee and to the full expert panel for review and approval.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Carcinoembryonic Antigen (CEA) as a Marker for Colorectal Cancer

A study from the Eastern Cooperative Oncology Group followed patients on INT 0089 after surgical resection for high-risk stage B2 and C colon carcinoma. For the 421 patients who developed recurrent disease, investigators tried to determine which tests were the most effective and cost-effective in detecting metastases. Follow-up testing was done by protocol guidelines. Ninety-six of the 421 patients with recurrent disease underwent surgical resection with curative intent. For the subgroup of resectable patients, the first test to detect recurrence was CEA, chest x-ray, colonoscopy, and other tests. The physician´s examination was unsuccessful in finding resectable disease. CEA was the most cost-effective approach to detecting potentially resectable metastases from colon cancer. Another study followed patients with a specified testing strategy after curative colorectal surgery. Here, 64% of recurrences were detected first by CEA, far more than the other tests in the battery.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The content of the guidelines and the manuscript were reviewed and approved by the Health Services Research Committee and by the ASCO Board.

The 2000 updated recommendations were validated through external review by the ASCO's Health Services Research Committee and by ASCO's Board of Directors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Colorectal Cancer

Carcinoembryonic Antigen as a Marker for Colorectal Cancer

1a. Carcinoembryonic antigen (CEA) is not recommended to be used as a screening test for colorectal cancer.

1b. Carcinoembryonic antigen may be ordered preoperatively in patients with colorectal carcinoma if it would assist in staging and surgical treatment planning. Although elevated preoperative carcinoembryonic antigen (> 5 mg/mL) may correlate with poorer prognosis, data are insufficient to support the use of carcinoembryonic antigen to determine whether to treat a patient with adjuvant therapy.

1c. If resection of liver metastases would be clinically indicated, it is recommended that postoperative serum carcinoembryonic antigen testing may be performed every 2 to 3 months in patients with stage II or III disease for 2 or more years after diagnosis. An elevated carcinoembryonic antigen, if confirmed by retesting, warrants further evaluation for metastatic disease, but does not justify the institution of adjuvant therapy or systemic therapy for presumed metastatic disease.

1d. Present data are insufficient to recommend routine use of the serum carcinoembryonic antigen alone for monitoring response to treatment. If no other simple test is available to indicate a response, carcinoembryonic antigen should be measured at the start of treatment for metastatic disease, and every 2 to 3 months during active treatment. Two values above baseline are adequate to document progressive disease, even in the absence of corroborating radiographs. Carcinoembryonic antigen is regarded as the marker of choice for monitoring colorectal cancer.

Lipid-Associated Sialic Acid as a Marker for Colorectal Cancer

2. Present data are insufficient to recommend lipid-associated sialic acid (LASA) for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

Cancer Antigen (CA) 19-9 as a Marker for Colorectal Cancer

3. Present data are insufficient to recommend cancer antigen (CA) 19-9 for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

DNA Ploidy or Flow Cytometric Proliferation Analysis as a Marker for Colorectal Cancer

4. Present data are insufficient to recommend DNA flow cytometrically-derived ploidy (DNA index) for the management of colorectal cancer.

p53 as a Marker for Colorectal Cancer

5. Present data are insufficient to recommend the use of p53 expression or mutation for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

ras as a Marker for Colorectal Cancer

6. Present data are insufficient to recommend the use of the ras oncogene for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

Breast Cancer

Cancer Antigen (CA) 15-3 as a Marker for Breast Cancer

1. Present data are insufficient to recommend cancer antigen 15-3 or cancer antigen 27.29 for screening, diagnosis, staging, or surveillance following primary treatment. Although a rising cancer antigen 15-3 or cancer antigen 27.29 level can detect recurrence following primary treatment, the clinical benefit is not established; therefore, it cannot be recommended. Options for therapy, however, remain unchanged, and there has been no demonstrated impact on the most significant outcomes (improved disease-free or overall survival, better quality of life, lesser toxicity, or improved cost-effectiveness) (American Society of Clinical Oncology, 1996). The data used by the Food and Drug Administration (FDA) to approve cancer antigen 27.29 were available to the panel previously; although the assay was approved by the FDA, the FDA does not require tests to show clinical benefit. Given the small body of evidence and until there is evidence of clinical benefit, present data are insufficient to recommend routine use of cancer antigen 27.29.

Carcinoembryonic Antigen as a Marker for Breast Cancer

2a. Carcinoembryonic antigen is not recommended for screening, diagnosis, staging, or routine surveillance of breast cancer patients after primary therapy.

2b. Routine use of carcinoembryonic antigen for monitoring response of metastatic disease to treatment is not recommended. However, in the absence of readily measurable disease, an increasing CEA may be used to suggest treatment failure.

Estrogen Receptors and Progesterone Receptors as Markers for Breast Cancer

3. Estrogen and progesterone receptors are recommended to be measured on every primary breast cancer, and may be measured on metastatic lesions if the results would influence treatment planning. In both premenopausal and postmenopausal patients, steroid hormone receptor status may be used to identify patients most likely to benefit from endocrine forms of adjuvant therapy and therapy for recurrent or metastatic disease.

DNA Flow Cytometrically-Derived Parameters as Markers for Breast Cancer

4a. Present data are insufficient to recommend obtaining DNA flow cytometry-derived estimates of DNA content or S-phase in breast tissue.

4b. DNA flow cytometry-derived ploidy are not recommended to be used to assign a patient to prognostic groupings. There is insufficient evidence to recommend the use of S-phase determination for assigning patients to prognostic groupings.

c-erbB-2 (HER-2/neu) as a Marker for Breast Cancer

5a. Present data are insufficient to recommend the use of c-erbB-2 (HER-2/neu) gene amplification or overexpression for management of patients with breast cancer.

2000 Recommendation: c-erbB-2 overexpression should be evaluated on every primary breast cancer either at the time of diagnosis or at the time of recurrence. Measures of c-erbB-2 amplification may also be of value.

Methods for Measuring c-erbB-2

5b. 2000 Recommendation: Because of the uncertain interchangeability, reproducibility, and clinical utility of different c-erbB-2 tests, it is important that clinical laboratories report not only an estimate c-erbB-2 but also a statement about the test's quality controls, the method, the specific kit or critical reagents, details of the scoring system, a statement regarding reproducibility, sensitivity, and specificity of the assay, and a reference to the clinical validation of the assay or its correlation with a clinically validated c-erbB-2 test.

Sensitivity to Trastuzumab

6. 2000 Recommendation: High levels of c-erbB-2 expression or c-erbB-2 amplification can be used to identify patients for whom trastuzumab may be of benefit for the treatment of metastatic, recurrent, and/or treatment-refractory unresectable locally advanced breast cancer.

Response to Cyclophosphamide/Methotrexate/Fluorouracil or Nonanthracycline-Based Adjuvant Chemotherapy

7. 2000 Recommendation: The question of whether c-erbB-2 overexpression affects the relative benefit of adjuvant cyclophosphamide methotrexate, and fluorouracil chemotherapy remains open, and the update committee cannot make a definitive practice recommendation at present.

Response to Anthracycline-Based Adjuvant Chemotherapy

8. 2000 Recommendation: High levels of c-erbB-2 expression, as determined by immunohistochemistry, may identify patients who particularly benefit from anthracycline-based adjuvant therapy, but levels of c-erbB-2 expression should not be used to exclude patients from anthracycline treatment.

Sensitivity to Endocrine Therapy

9. 2000 Recommendation: The use of c-erbB-2 data to decide whether to prescribe endocrine therapy either in the adjuvant or metastatic setting is not recommended.

Sensitivity or Resistance to Taxane Therapy

10. 2000 Recommendation: The use of c-erbB-2 data to decide whether to prescribe taxane-based chemotherapy either in the adjuvant or metastatic setting is not recommended.

Use of Measures of c-erbB-2 to Predict Patient Prognosis

11. 2000 Recommendation: The data are insufficient to recommend the routine use of c-erbB-2 overexpression in patients with early breast cancer.

Utility of Measures of Circulating Extracellular Domain of c-erbB-2

12. 2000 Recommendation: Measuring circulating extracellular domain of c-erbB-2 is not currently recommended for any clinical setting.

p53 as a Marker for Breast Cancer

13. Present data are insufficient to recommend use of p53 measurements for management of patients with breast cancer.

Cathepsin-D as a Marker for Breast Cancer

14. Present data are insufficient to recommend use of cathepsin-D measurements for management of patients with breast cancer.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Level I analyses and trials have rarely been performed to evaluate tumor markers.

The Panel made every effort to develop these guideline using evidence-based deliberations. Wide variation in established practice, with limited data for or against the use of a particular marker, made some guidelines difficult to formulate. In the absence of data from well-performed studies, current use in clinical practice was also considered. The latter was, however, never regarded as the sole criterion for a recommendation if published data contradicted current practice patterns.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improvements in the prevention, screening, treatment, and surveillance of breast and colorectal cancers.

POTENTIAL HARMS

Harms considered were inappropriate disease management, and excess cost without definable benefit.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. The American Society of Clinical Oncology considers adherence to these guidelines to be voluntary. The ultimate determination regarding their application is to be made by the physician in light of each patient's individual circumstances. In addition, these guidelines describe administration of therapies in clinical practice; they cannot be assumed to apply to interventions performed in the context of clinical trials, given that such clinical studies are designed to test innovative and novel therapies in which better treatment is of paramount importance.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Bast RC, Ravdin P, Hayes DF, Bates S, Fritsche H, Jessup JM, Kemeny N, Locker GY, Mennel RG, Somerfield MR. 2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001 Mar 15;19(6):1865-78.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 (revised 2001 Mar)

GUIDELINE DEVELOPER(S)

American Society of Clinical Oncology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Clinical Oncology (ASCO)

GUIDELINE COMMITTEE

American Society of Clinical Oncology (ASCO) Tumor Markers Expert Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Expert Panel Members: Robert C. Bast, Jr, MD; Susan Bates, MD; Herbert Fritsche, Jr, MD; Daniel F. Hayes, MD; John Jessup, MD; Nancy E. Kemeny, MD; Gershon Y. Locker, MD; Robert G. Mennel, MD; Peter Ravdin, MD; Mark R. Somerfield, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline. This guideline updates the 1997 recommendations issued by the American Society of Clinical Oncology (ASCO) - 1997 update of recommendations for the use of tumor markers in breast and colorectal cancer. Adopted on November 7, 1997 by the American Society of Clinical Oncology. J Clin Oncol 1998 Feb;16[2]:793-5).

ASCO guidelines are updated annually by a Review Committee of the full Guidelines Expert Panel, and every 3 years by the full Panel.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Previous versions of the guideline are available from the American Society of Clinical Oncology (ASCO) Web site:

- 1997 Update of Recommendations for the Use of Tumor Markers in Breast and Colorectal Cancer.
- Tumor Markers in Breast and Colorectal Cancer.

Print copies: Available from American Society of Clinical Oncology, Health Services Research, 1900 Duke Street, Suite 200, Alexandria, VA 22314.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

A document titled "Understanding Tumor Markers for Breast and Colorectal Cancers" is available from the American Society for Clinical Oncology (ASCO) Web site.

has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on May 25, 2001. It was verified by the guideline developer as of September 7, 2001.

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